Rx Only

# cobas® SARS-CoV-2 Duo

## Qualitative and quantitative assay for use on the cobas® 6800/8800 Systems

*For use under the Emergency Use Authorization (EUA) only.*
For in vitro diagnostic use

| | |
|---|---|
| **cobas® SARS-CoV-2 Duo** | P/N: 09500111190 |
| **cobas® SARS-CoV-2 Duo Control Kit** | P/N: 09500120190 |
| **cobas® Buffer Negative Control Kit** | P/N: 07002238190 |

# Table of contents

# Intended use

**cobas**® SARS-CoV-2 Duo for use on the **cobas**® 6800/8800 Systems (**cobas**® SARS CoV 2 Duo) is an automated real-time RT-PCR assay for the qualitative detection of SARS-CoV-2 RNA in healthcare provider instructed self-collected nasal (anterior nares and mid-turbinate) swab specimens (collected on site), and healthcare provider-collected nasal (anterior nares and mid-turbinate) and nasopharyngeal swab specimens collected from individuals suspected of COVID-19 by their healthcare provider. This assay also performs quantitation of SARS-CoV-2 RNA levels in the collected specimen; however, only the qualitative result of **cobas**® SARS-CoV-2 Duo is intended for use as an aid in the diagnosis of SARS-CoV-2 infection in patients suspected of COVID-19 by their healthcare provider. **cobas**® SARS-CoV-2 Duo is for use only under Emergency Use Authorization (EUA) in laboratories certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high or moderate complexity tests.

Results are for the detection of SARS-CoV-2 RNA. SARS-CoV-2 RNA is generally detectable in nasal (anterior nares and mid-turbinate) and nasopharyngeal swab specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA. At this time, correlation of viral load with a specific clinical diagnosis, prognosis or patient management decision has not been clinically established. Patient management should therefore be based on the qualitative result upon consideration of clinical observation, patient history and other diagnostic information. The numerical values for the viral load are for information only. Positive results do not rule out bacterial infection or co-infection with other viruses.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, recent exposures and epidemiological information. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities. **cobas**® SARS-CoV-2 Duo is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and on the use of the **cobas**® 6800/8800 Systems. **cobas**® SARS-CoV-2 Duo is only for use under the Food and Drug Administration's Emergency Use Authorization.

# Summary and explanation of the test

### Explanation of the test

cobas® SARS-CoV-2 Duo is an automated real-time RT-PCR assay for the in vitro qualitative and quantitative detection of SARS-CoV-2 RNA in collected nasal and nasopharyngeal swab specimens collected in Copan Universal Transport Medium System (UTM-RT) or BD™ Universal Viral Transport System (UVT) from individuals suspected of COVID-19. The viral load is quantified against a non-SARS-CoV-2 armored RNA quantitation standard (RNA-QS), which is introduced into each specimen during sample preparation. The RNA-QS also functions as an internal control to monitor the entire sample preparation and PCR amplification process. In addition, the test utilizes three external controls: a high titer positive, a low titer positive, and a negative control. The high positive and low positive external controls are manufactured by dilution from stock material with a titer traceable to the First WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146). Each **cobas**® SARS-CoV-2 Duo kit lot is calibrated traceable to the First WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146).

## Principles of the procedure

**cobas**® SARS-CoV-2 Duo is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The **cobas**® 6800/8800 Systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by the **cobas**® 6800/8800 software, which assigns results for all tests. Results can be reviewed directly on the system screen, and printed as a report.

Nucleic acid from patient samples and added RNA-QS molecules are simultaneously extracted. Nucleic acid is released by addition of proteinase and lysis reagent to the sample. The released nucleic acid binds to the silica surface of the added magnetic glass particles. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors, are removed with subsequent wash steps and purified nucleic acid is eluted from the magnetic glass particles with elution buffer at elevated temperature.

External controls are processed in the same way with each **cobas**® SARS-CoV-2 Duo run. The test utilizes three external controls: a high titer positive, a low titer positive, and a negative control.

Selective amplification of SARS-CoV-2 target nucleic acid from the sample is achieved by the use of a dual target virus specific approach from highly-conserved regions of SARS-CoV-2 located in the ORF 1a and ORF 1a/b non-structural regions. Selective amplification of RNA QS is achieved by the use of non-competitive sequence specific forward and reverse primers which have no homology with the SARS-CoV-2 genome.

A thermostable DNA polymerase enzyme is used for amplification. The target and RNA QS sequences are amplified simultaneously utilizing a universal PCR amplification profile with pre-defined temperature steps and number of cycles.

The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythimidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon). Any contaminating amplicons from previous PCR runs are destroyed by the AmpErase enzyme [uracil-N-glycosylase], which is included in the PCR mix, when heated in the first thermal cycling step. However, newly formed amplicons are not destroyed since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

Amplified target is detected by cleavage of fluorescently labeled oligonucleotide probes. The **cobas**® SARS-CoV-2 Duo master mix contains two detection probes specific for SARS-CoV-2 target sequences and one for the RNA QS. The probes are labeled with target-specific fluorescent reporter dyes allowing simultaneous detection of SARS-CoV-2 target and RNA QS in two different target channels. The fluorescent signal of the intact probe is suppressed by the quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage by the 5' to 3' nuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye increases concomitantly. Real-time detection and discrimination of PCR products are accomplished by measuring the fluorescence of the released reporter dyes for the viral targets and RNA QS.

# Reagents and materials

The materials provided for **cobas**® SARS-CoV-2 Duo can be found in Table 1. Materials required, but not provided can be found in Table 2, Table 3, Table 4, Table 7, and Table 8.

Refer to the **Reagents and materials** section and **Precautions and handling requirements** section for the hazard information for the product.

## cobas® SARS-CoV-2 Duo reagents and controls

All unopened reagents and controls shall be stored as recommended in Table 1 to Table 4.

**Table 1 cobas**® SARS-CoV-2 Duo

**(SARS-CoV-2 Duo)**

Store at 2-8°C
192 test cassette (P/N 09500111190)

| Kit components | Reagent ingredients | Quantity per kit 192 tests |
|---|---|---|
| **Proteinase Solution (PASE)** | Tris buffer, < 0.05% EDTA, calcium chloride, calcium acetate, 8% proteinase, glycerol<br><br>EUH210: Safety data sheet available on request.<br>EUH208: Contains Subtilisin from Bacillus subtilis. May produce an allergic reaction. | 22.3 mL |
| **RNA Quantitation Standard (RNA-QS)** | Tris buffer, < 0.05% EDTA, < 0.001% non-Sarbecovirus related armored RNA construct containing primer and probe specific primer sequence regions (non-infectious RNA in MS2 bacteriophage), < 0.1% sodium azide | 21.2 mL |
| **Elution Buffer (EB)** | Tris buffer, 0.2% methyl-4 hydroxybenzoate | 21.2 mL |
| **Master Mix Reagent 1 (MMX-R1)** | Manganese acetate, potassium hydroxide, < 0.1% sodium azide | 7.5 mL |
| **SARS-CoV-2 Duo Master Mix Reagent 2 (SARS-CoV-2 Duo MMX-R2)** | Tricine buffer, potassium acetate, < 18% dimethyl sulfoxide, glycerol, < 0.1% Tween 20, EDTA, < 0.12% dATP, dCTP, dGTP, dUTPs, < 0.01% upstream and downstream SARS-CoV-2 primers, < 0.01% Internal Control forward and reverse primers, < 0.01% fluorescent-labeled oligonucleotide probes specific for SARS-CoV-2 and the RNA Internal Control, < 0.01% oligonucleotide aptamer, < 0.1% Z05D DNA polymerase, < 0.10% AmpErase (uracil-N-glycosylase) enzyme (microbial), < 0.1% sodium azide | 9.7 mL |

**Table 2 cobas®** SARS-CoV-2 Duo Control Kit

**(SARS-CoV-2 Duo CTL)**

Store at 2–8°C
(P/N 09500120190)

| Kit components | Reagent ingredients | Quantity per kit |
|---|---|---|
| **SARS-CoV-2 Low Positive Control (SARS-CoV-2 L(+)C)** | Tris buffer, < 0.05% Sodium azide, < 0.005% EDTA, < 0.003% Poly rA, < 0.01% Non-infectious plasmid DNA (microbial) containing SARS-CoV-2 sequence | 5.2 mL (8 x 0.65 mL) |
| **SARS-CoV-2 High Positive Control (SARS-CoV-2 H(+)C)** | Tris buffer, < 0.05% Sodium azide, < 0.005% EDTA, < 0.003% Poly rA, < 0.01% Non-infectious plasmid DNA (microbial) containing SARS-CoV-2 sequence | 5.2 mL (8 x 0.65 mL) |

**Table 3 cobas®** Buffer Negative Control Kit

Store at 2-8°C
(P/N 07002238190)

| Kit components | Reagent ingredients | Quantity per kit |
|---|---|---|
| **cobas® Buffer Negative Control (BUF (-) C)** | Tris buffer, < 0.1% sodium azide, EDTA, < 0.002% Poly rA RNA (synthetic) | 16 mL (16 x 1 mL) |

# cobas omni reagents for sample preparation

**Table 4 cobas omni** reagents for sample preparation*

| Reagents | Reagent ingredients | Quantity per kit | Safety symbol and warning** |
|---|---|---|---|
| **cobas omni MGP Reagent (MGP)**<br>Store at 2–8°C<br>(P/N 06997546190) | Magnetic glass particles, Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide | 480 tests | Not applicable |
| **cobas omni Specimen Diluent (SPEC DIL)**<br>Store at 2–8°C<br>(P/N 06997511190) | Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide | 4 x 875 mL | Not applicable |
| **cobas omni Lysis Reagent (LYS)**<br>Store at 2–8°C<br>(P/N 06997538190) | 43% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate | 4 x 875 mL |  <br>**DANGER**<br>H302 + H332: Harmful if swallowed or if inhaled.<br>H314: Causes severe skin burns and eye damage.<br>H411: Toxic to aquatic life with long lasting effects.<br>EUH032: Contact with acids liberates very toxic gas.<br>P273: Avoid release to the environment.<br>P280: Wear protective gloves/ protective clothing/ eye protection/ face protection/hearing protection.<br>P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.<br>P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor.<br>P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.<br>P391: Collect spillage.<br>593-84-0 Guanidinium thiocyanate<br>9002-92-0 Polidocanol<br>3483-12-3 (R*,R*)-1,4-dimercaptobutane-2,3-diol |
| **cobas omni Wash Reagent (WASH)**<br>Store at 15–30°C<br>(P/N 06997503190) | Sodium citrate dihydrate, 0.1% methyl-4 hydroxybenzoate | 4.2 L | Not applicable |

* These reagents are not included in the **cobas**® SARS-CoV-2 Duo test kits. See listing of additional materials required (Table 7).

** Product safety labeling primarily follows EU GHS guidance

***Hazardous substance

## Reagent storage and handling requirements

Reagents shall be stored and will be handled as specified in Table 5 and Table 6.

When reagents are not loaded on the **cobas**® 6800/8800 Systems, store them at the corresponding temperature specified in Table 5.

**Table 5** Reagent storage (when reagent is not on the system)

| Reagent | Storage temperature |
|---|---|
| **cobas**® SARS-CoV-2 Duo - 192T | 2–8°C |
| **cobas**® SARS-CoV-2 Duo Control Kit | 2–8°C |
| **cobas**® Buffer Negative Control Kit | 2–8°C |
| **cobas omni** Lysis Reagent | 2–8°C |
| **cobas omni** MGP Reagent | 2–8°C |
| **cobas omni** Specimen Diluent | 2–8°C |
| **cobas omni** Wash Reagent | 15–30°C |

Reagents loaded onto the **cobas**® 6800/8800 Systems are stored at appropriate temperatures and their expiration is monitored by the system. The **cobas**® 6800/8800 Systems allow reagents to be used only if all of the conditions shown in Table 6 are met. The system automatically prevents use of expired reagents. Table 6 allows the user to understand the reagent handling conditions enforced by the **cobas**® 6800/8800 Systems.

**Table 6** Reagent expiry conditions enforced by the **cobas**® 6800/8800 Systems

| Reagent | Kit expiration date | Open-kit stability | Number of runs for which this kit can be used | On-board stability (cumulative time on board outside refrigerator) |
|---|---|---|---|---|
| **cobas**® SARS-CoV-2 Duo | Date not passed† | 90 days from first usage† | Max 40 runs† | Max 40 hours† |
| **cobas**® SARS-CoV-2 Duo Control Kit | Date not passed† | Not applicable[a] | Not applicable | Max 8 hours† |
| **cobas**® Buffer Negative Control Kit | Date not passed | Not applicable[a] | Not applicable | Max 10 hours |
| **cobas omni** Lysis Reagent | Date not passed | 30 days from loading* | Not applicable | Not applicable |
| **cobas omni** MGP Reagent | Date not passed | 30 days from loading* | Not applicable | Not applicable |
| **cobas omni** Specimen Diluent | Date not passed | 30 days from loading* | Not applicable | Not applicable |
| **cobas omni** Wash Reagent | Date not passed | 30 days from loading* | Not applicable | Not applicable |

[a] Single use reagents

*Time is measured from the first time that reagent is loaded onto the **cobas**® 6800/8800 Systems.

† The performance has not been established for suggested use cycles and time, but is based on similar reagents used on the same system.

# Additional materials required

**Table 7** Materials and consumables for use on **cobas**® 6800/8800 Systems

| **Material** | **P/N** |
|---|---|
| **cobas omni** Processing Plate | 05534917001 |
| **cobas omni** Amplification Plate | 05534941001 |
| **cobas omni** Pipette Tips | 05534925001 |
| **cobas omni** Liquid Waste Container | 07094388001 |
| **cobas omni** Lysis Reagent | 06997538190 |
| **cobas omni** MGP Reagent | 06997546190 |
| **cobas omni** Specimen Diluent | 06997511190 |
| **cobas omni** Wash Reagent | 06997503190 |
| Solid Waste Bag and Solid Waste Container<br>or<br>Solid Waste Bag With Insert and Kit Drawer | 07435967001 and 07094361001<br>or<br>08030073001 and 08387281001 |
| **cobas omni** Secondary Tubes 13x75 (optional) | 06438776001 |

## Instrumentation and software required

The **cobas**® 6800/8800 Systems software and **cobas**® SARS-CoV-2 Duo analysis package must be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system.

**Table 8** Instrumentation

| Equipment | P/N |
|---|---|
| **cobas**® 6800 System (Option Moveable) | 05524245001 and 06379672001 |
| **cobas**® 6800 System (Fix) | 05524245001 and 06379664001 |
| **cobas**® 8800 System | 05412722001 |
| Sample Supply Module | 06301037001 |
| Instrument Gateway | 06349595001 |

For additional information, please refer to the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide.

Note: Contact your local Roche representative for a detailed order list for sample racks, racks for clotted tips and rack trays accepted on the instruments.

# Precautions and handling requirements

## Warnings and precautions

As with any test procedure, good laboratory practice is essential to the proper performance of this assay. Due to the high sensitivity of this test, care should be taken to keep reagents and amplification mixtures free of contamination.

- For in vitro diagnostic use under Emergency Use Authorization only.
- This product has not been FDA cleared or approved.
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens.
- This product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization (EUA) for use by authorized laboratories; use by laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests.
- This product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
- Positive results are indicative of the presence of SARS-CoV-2 RNA.
- Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.
- All patient samples should be handled as if infectious, using good laboratory procedures as outlined in Biosafety in Microbiological and Biomedical Laboratories and in the CLSI Document M29-A4.[1,2] Only personnel proficient in handling infectious materials and the use of **cobas**® SARS-CoV-2 Duo and **cobas**® 6800/8800 Systems should perform this procedure.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, immediately disinfect with a freshly prepared solution of 0.6% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10) or follow appropriate site procedures.
- The use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect optimal test performance.
- False positive results may occur if carryover of samples is not adequately controlled during sample handling and processing.

## Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples or controls.
- Before use, visually inspect each reagent cassette, diluent, lysis reagent, and wash reagent to ensure that there are no signs of leakage. If there is any evidence of leakage, do not use that material for testing.
- **cobas omni** Lysis Reagent contains guanidine thiocyanate, a potentially hazardous chemical. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- **cobas**® SARS-CoV-2 Duo kit, **cobas**® SARS-CoV-2 Duo Control kit, **cobas**® Buffer Negative Control kit, **cobas omni** MGP Reagent, and **cobas omni** Specimen Diluent contain sodium azide as a preservative. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur. If these reagents are spilled, dilute with water before wiping dry.
- Do not allow **cobas omni** Lysis Reagent, which contains guanidine thiocyanate, to contact sodium hypochlorite (bleach) solution. This mixture can produce a highly toxic gas.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.

## Good laboratory practice

- Do not pipette by mouth.
- Do not eat, drink, or smoke in designated work areas.
- Wear laboratory gloves, laboratory coats, and eye protection when handling samples and reagents. Gloves must be changed between handling samples and **cobas**® SARS-CoV-2 Duo kits, **cobas**® SARS-CoV-2 Duo Control kit, **cobas**® Buffer Negative Control kit and **cobas omni** reagents to prevent contamination. Avoid contaminating gloves when handling samples and controls.
- Wash hands thoroughly after handling samples and kit reagents, and after removing the gloves.
- Thoroughly clean and disinfect all laboratory work surfaces with a freshly prepared solution of at least 0.6% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10). Follow by wiping the surface with 70% ethanol.
- If spills occur on the **cobas**® 6800/8800 instrument, follow the instructions in the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide to properly clean and decontaminate the surface of instrument(s).

# Sample collection, transport, and storage

**Note: Handle all samples and controls as if they are capable of transmitting infectious agents.**

## Sample collection

Ensure that the correct collection device is used with the appropriate sample type by referring to the table below:

**Table 9** Overview of collection devices and sample types

| **Collection Device** | **Sample Type**<br><br>Nasopharyngeal | **Sample Type**<br><br>Nasal (Anterior Nares and Mid-Turbinate) |
|---|---|---|
| Copan Universal Transport Media (UTM-RT) | √ | √ |
| BD™ Universal Viral Transport (UVT) | √ | √ |

- Collect nasal (anterior nares and mid-turbinate) and nasopharyngeal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT) or BD™ Universal Viral Transport (UVT).
- Refer to the Instructions for Use of the Collection Devices for hazard information.

## Transport and storage

- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.
- Samples collected in UTM-RT or BD™ Universal Viral Transport (UVT):
    - After collection, specimens can be stored for up to 24 hours at 2-25°C followed by up to 3 days at 2-8°C and at ≤ -70°C for up to 30 days.
    - Specimen are stable for up to two freeze/thaw cycles when frozen at ≤ -70°C.

# Instructions for use

## Procedural notes

- Do not use **cobas**® SARS-CoV-2 Duo reagents, **cobas**® SARS-CoV-2 Duo Control Kit, **cobas**® Buffer Negative Control Kit, or **cobas omni** reagents after their expiry dates.
- Do not reuse consumables. They are for one-time use only.
- Refer to the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide for proper maintenance of instruments.

## Running cobas® SARS-CoV-2 Duo

**cobas**® SARS-CoV-2 Duo can be run with a minimum required sample volume of 0.6 mL in the **cobas omni** secondary tube for specimens collected in Copan Universal Transport Medium (UTM-RT) and BD™ Universal Viral Transport (UVT).

## Specimens collected in UTM-RT or UVT

Specimens can be collected in Copan Universal Transport Medium (UTM-RT) or BD™ Universal Viral Transport (UVT) tubes.

Specimens collected in tubes compatible with **cobas**® 6800/8800 Systems may be loaded directly onto the **cobas**® 6800/8800 Systems. The swab must be removed from the sample tube prior to direct loading onto the system. Specimens collected in tubes which are not compatible with the **cobas**® 6800/8800 Systems must be transferred into a secondary tube prior to processing on the **cobas**® 6800/8800 Systems. The **cobas omni** Secondary Tube is the preferred option.

Additional tubes for testing with **cobas**® SARS-CoV-2 Duo are available. Contact your local Roche representative for detailed testing instructions and an order list of primary tubes and secondary tubes compatible with the instruments.

***Always use caution when transferring specimens from a primary collection tube to a secondary tube.***

***Use pipettes with aerosol-barrier or positive-displacement tips to handle specimens.***

***Always use a new pipette tip for each specimen***.

***Ensure samples are equilibrated to room temperature prior to transfer into a cobas omni Secondary Tube.***

Follow the steps below to transfer patient sample from a primary collection tube into a **cobas omni** Secondary Tube:

- Unscrew the primary sample tube cap.
- Lift the cap and any attached swab to allow a pipette to be inserted into the sample tube.
- Transfer 0.6 mL into the prepared barcoded secondary tube.
- Transfer secondary tube to a rack. Close the primary sample tube cap.

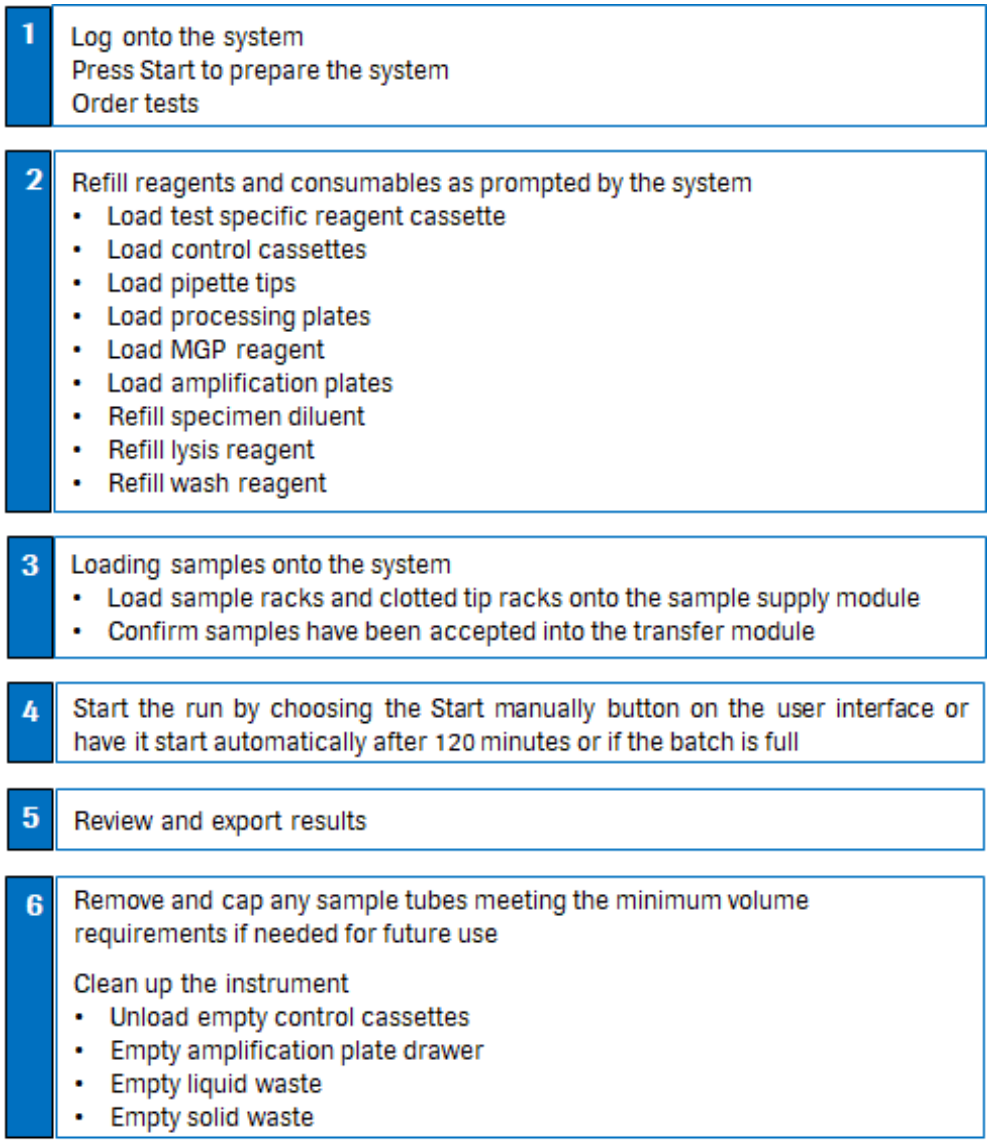
**Table 10** Sample type selection in the user interface of the **cobas**® SARS-CoV-2 Duo

| Collection kit/Matrix type | Minimum volume (mL)<br>Processing tube | Process as Sample Type |
|---|---|---|
| Copan Universal Transport Medium<br>BD™ Universal Viral Transport | 0.6 mL<br>**cobas omni** Secondary tube | VTM |

## cobas® SARS-CoV-2 Duo procedure

The test procedure is described in detail in the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide. Figure 1 below summarizes the procedure.

**Figure 1** **cobas**® SARS-CoV-2 Duo procedure



# Results

The **cobas**® 6800/8800 Systems automatically detect SARS-CoV-2 RNA and determine the RNA concentration, for each sample and control. Individual target results for samples as well as test validity and overall results for controls are displayed on the user interface. SARS-CoV-2 RNA concentration is expressed in International Units per milliliter (IU/mL).

## Quality control and validity of results

- One **cobas**® Buffer Negative Control [(-) Ctrl] and two positive controls, a low positive control [SARS-CoV-2 L (+) C] and a high positive control [SARS-CoV-2 H (+) C] are processed with each batch.
- In the **cobas**® 6800/8800 software and/or report, check for flags and their associated results to ensure the batch validity.
- All flags are described in the **cobas**® 6800/8800 Systems User Guide.
- The batch is valid if no flags appear for any controls. If the batch is invalid, repeat testing of the entire batch.

Validation of results is performed automatically by the **cobas**® 6800/8800 software based on negative and positive control performance.

## Interpretation of results

Test results are reported as positive or negative. Positive results are reported along with a numeric value for the quantity of SARS-CoV-2 viral RNA in IU/mL if the RNA levels are between 100 IU/mL and 1.00E+09 IU/mL (=1,000,000,000 IU/mL). Positive results of samples that are detected but for which the numeric results are below the LLoQ of 100 IU/mL are low positive samples that are reported as detected < Titer min. Positive results of samples that are detected with a numeric result above 1.00E+09 IU/mL are high positive samples that are reported as detected > Titer max.

Display examples for **cobas**® SARS-CoV-2 Duo are shown in Figure 2.

**Figure 2** Example of **cobas**® SARS-CoV-2 Duo results display

| Test | Sample ID | Valid | Flags | Sample Type | Overall Result | Target 1 (Quantitative)** | Target 2 (Qualitative)** |
|---|---|---|---|---|---|---|---|
| SARS-CoV-2-Duo | Sample_01 | Yes | | VTM | Target Not Detected | Target Not Detected | Negative |
| SARS-CoV-2-Duo | Sample_02 | No | Y40T | VTM | Invalid | Invalid | Invalid |
| SARS-CoV-2-Duo | Sample_03 | Yes | | VTM | Titer | 4.87e+007 IU/ml* | Positive |
| SARS-CoV-2-Duo | Sample_04 | Yes | | VTM | > Titer max | > Titer max | Positive |
| SARS-CoV-2-Duo | Sample_05 | Yes | | VTM | < Titer min | < Titer min | Positive |
| SARS-CoV-2-Duo | C1614202840904288 28404 | Yes | | SARS-CoV-2 H (+) C | Titer | 1.16e+007 IU/ml* | Valid |
| SARS-CoV-2-Duo | C1614202840930095 80264 | Yes | | SARS-CoV-2 L (+) C | Titer | 1.31e+003 IU/ml* | Valid |
| SARS-CoV-2-Duo | C1614202840930095 54953 | Yes | | (-) Ctrl | Target Not Detected | Target Not Detected | Valid |

* Illustrative titer values

** The Target 1 and Target 2 labels reflect the user interface on the system and do not relate to the analyte targets. Target 1 represents the quantitative viral load values and Target 2 represents the qualitative SARS-CoV-2 result.

For a valid batch, check each individual sample for flags in the **cobas**® 6800/8800 software and/or report. The result interpretation should be as follows:

A valid batch may include both valid and invalid sample results.

At this time, correlation of viral load with a specific clinical diagnosis, prognosis, or patient management decision has not been clinically established. Patient management should therefore be based on the qualitative result upon consideration of clinical observation, patient history and other diagnostic information. The numerical values for the viral load are for information only.

**Table 11** Target results for individual target result interpretation

| Results (quantitative) | Results (qualitative) | Interpretation |
|---|---|---|
| Target Not Detected | Negative | SARS-CoV-2 RNA not detected.<br>Report results as "SARS-CoV-2 not detected." |
| < Titer min[a] | Positive | SARS-CoV-2 RNA is detected.<br>The sample is very low positive with a calculated titer below the Lower Limit of Quantitation (LLoQ) of the assay.<br>Report results as "SARS-CoV-2 detected, less than (Titer min)."<br>Titer min = 100 IU/mL |
| Titer (IU/mL)[b] | Positive | SARS-CoV-2 RNA is detected.<br>The sample is positive with a calculated titer within the Linear Range of the assay – between 100 and 1,000,000,000 IU/mL.<br>Report results as "(Titer) of SARS-CoV-2 detected." |
| > Titer max[c] | Positive | SARS-CoV-2 RNA is detected.<br>The sample is very high positive with a calculated titer above the Upper Limit of Quantitation (ULoQ) of the assay.<br>Report results as "SARS-CoV-2 detected, greater than (Titer max)."<br>Titer max = 1.00E+09 IU/mL (1,000,000,000 IU/mL) |
| Invalid | Invalid | Results are invalid.<br>Sample should be retested. If the result is still invalid, report as invalid. A new specimen should be obtained. |

[a] A sample result of "< Titer min" indicates a positive sample that has a very low SARS-CoV-2 RNA level below 100 IU/mL and can therefore not be quantified. Patient management decisions should not be based on numerical values for the SARS-CoV-2 viral load.

[b] A sample result with a numeric titer between 100 and 1,000,000,000 IU/mL indicates a positive sample that has a SARS-CoV-2 RNA level within the linear range of the test. Patient management decisions should not be based on numerical values for the SARS-CoV-2 viral load.

[c] A sample result "> Titer max" indicates a positive samplethat has a very high RNA level above 1,000,000,000,IU/mL and can therefore not be quantified. If a quantitative result is desired, the original sample should be diluted with SARS-CoV-2-negative transport media depending on the type of the original sample, and the test should be repeated. Multiply the reported result by the dilution factor. Patient management decisions should not be based on numerical values for the SARS-CoV-2 viral load.

## Procedural limitations

- **cobas**® SARS-CoV-2 Duo has been evaluated only for use in combination with the **cobas**® SARS-CoV-2 Duo Control Kit, **cobas**® Buffer Negative Control Kit, **cobas omni** MGP Reagent, **cobas omni** Lysis Reagent, **cobas omni** Specimen Diluent, and **cobas omni** Wash Reagent for use on the **cobas**® 6800/8800 Systems.
- Clinical utility of the **cobas**® SARS-CoV-2 Duo quantitative result has not been established. The clinical meaning of samples with "SARS-CoV-2 detected, less than (Titer min)." and "SARS-CoV-2 detected, greater than (Titer max)." results is unknown.
- Patient management decisions should be based on the qualitative test result with the **cobas**® SARS-CoV-2 Duo (positive or negative) and upon consideration of clinical observations, patient history and other diagnostic information.
- Reliable results depend on proper sample collection, storage and handling procedures.
- This test can be used for the detection of SARS-CoV-2 RNA in nasal (anterior nares and mid-turbinate), and nasopharyngeal swab samples collected in a Copan UTM-RT System (UTM-RT) or BD™ Universal Viral Transport System (UVT). Testing of other sample types with **cobas**® SARS-CoV-2 Duo may result in inaccurate results.
- Detection of SARS-CoV-2 RNA may be affected by sample collection methods, patient factors (e.g., presence of symptoms), and/or stage of infection.
- As with any molecular test, mutations within the target regions of **cobas**® SARS-CoV-2 Duo could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next, users perform method correlation studies in their laboratory to qualify technology differences. One hundred percent agreement between the results should not be expected due to aforementioned differences between technologies. Users should follow their own specific policies/procedures.
- False negative or invalid results may occur due to interference. The Quantitative Standard is included in **cobas**® SARS-CoV-2 Duo to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- The addition of AmpErase enzyme into the **cobas**® SARS-CoV-2 Duo Master Mix reagent enables selective amplification of target RNA; however, good laboratory practices and careful adherence to the procedures specified in this Instructions For Use document are necessary to avoid contamination of reagents.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

## Conditions of authorization for the laboratory

The **cobas**® SARS-CoV-2 Duo Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas.

To assist clinical laboratories running the **cobas**® SARS-CoV-2 Duo, the relevant Conditions of Authorization are listed verbatim below, and are required to be met by laboratories performing the EUA test.

### Authorized Laboratories

A. Authorized laboratories[1] using **cobas**® SARS-CoV-2 Duo must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
B. Authorized laboratories must report results clearly as "positive", "negative", or "invalid"; viral load values can be added to positive results. The laboratory must not report viral load values without also clearly identifying the result as positive.
C. Authorized laboratories using **cobas**® SARS-CoV-2 Duo must use the test as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use **cobas**® SARS-CoV-2 Duo are not permitted.
D. Authorized laboratories that receive **cobas**® SARS-CoV-2 Duo must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
E. Authorized laboratories using **cobas**® SARS-CoV-2 Duo must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
F. Authorized laboratories must collect information on the performance of **cobas**® SARS-CoV-2 Duo and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Roche Diagnostics US Customer Technical Support 1-800-526-1247 any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the test of which they become aware.
G. All operators using **cobas**® SARS-CoV-2 Duo must be appropriately trained in performing and interpreting the results of the test, use appropriate personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.
H. Roche Molecular Systems, Inc., its authorized distributor(s) and authorized laboratories using **cobas**® SARS-CoV-2 Duo must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records must be made available to FDA for inspection upon request.

[1]Authorized laboratories are laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high or moderate complexity tests.

# Non-clinical performance evaluation

## Key performance characteristics

### Analytical sensitivity (Limit of Detection)

The Limit of Detection (LoD) study determines the lowest detectable concentration of SARS-CoV-2 at which greater or equal to 95% of all (true positive) replicates test positive. The achieved LoD was 50 IU/mL based on hit rate analysis (25.8 IU/mL per Probit).

To determine the LoD, the WHO International Standard for SARS-CoV-2 (NIBSC code 20/146) was serially diluted in negative simulated clinical matrix stabilized in UTM-RT. Six concentration levels, with two-fold serial dilutions between the levels, were prepared on three days and tested with a total of 81 replicates per concentration across three reagent lots randomized with an additional 81 replicates of a blank sample (negative simulated clinical matrix stabilized in UTM-RT).

The results are shown in Table 12.

**Table 12** Summary LoD for all kit lots combined and individually

| Viral Strain | Kit Lot | Number of Positives/ Number of Valid Replicates | Hit rate ≥ 95% [IU/mL] | Hit rate ≥ 95% Mean Ct | 95% LoD PROBIT [IU/mL] | 95% confidence interval [IU/mL] |
|---|---|---|---|---|---|---|
| WHO International Standard for SARS-CoV-2 (NIBSC code 20/146) | combined | 77/81 | 25.0 | 38.2 | 24.1 | 19.3 - 32.8 |
| WHO International Standard for SARS-CoV-2 (NIBSC code 20/146) | Kit Lot 1 | 27/27 | 25.0 | 38.1 | 20.3 | 14.1 - 39.6 |
| WHO International Standard for SARS-CoV-2 (NIBSC code 20/146) | Kit Lot 2 | 27/27 | **50.0*** | 37.2 | **25.8*** | 18.0 - 48.0 |
| WHO International Standard for SARS-CoV-2 (NIBSC code 20/146) | Kit Lot 3 | 27/27 | 50.0 | 37.1 | 25.6 | 18.1 - 46.0 |

* Achieved LoD is based on the least performing lot

### Linear range

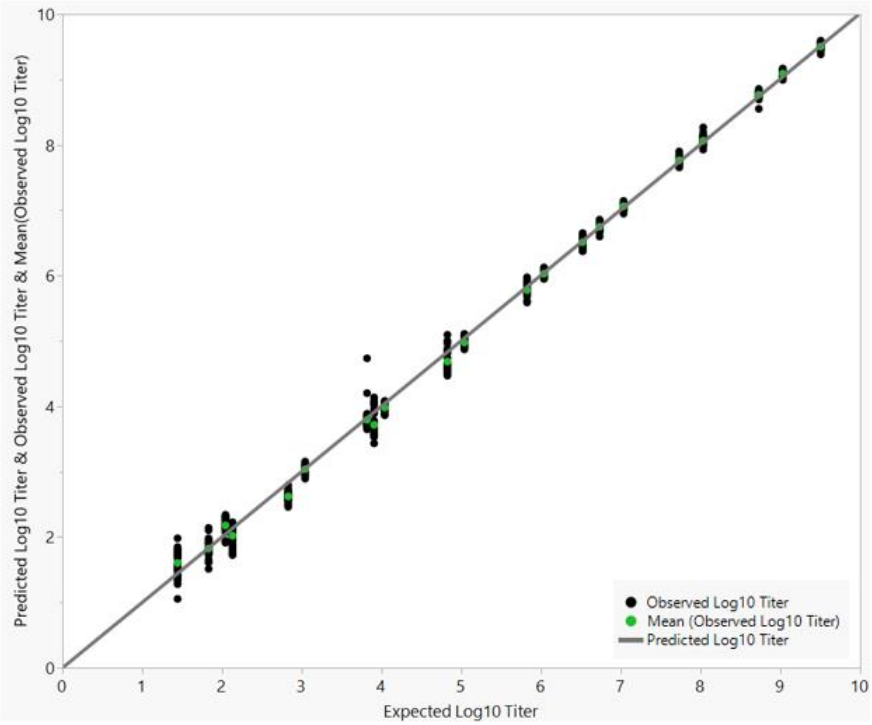
Linearity of **cobas**® SARS-CoV-2 Duo was evaluated using a dilution series consisting of 19 panel members with SARS-CoV-2 RNA spanning the assay linear range. A high titer aRNA stock was used to prepare 14 panel members spanning the entire linear range. A clinical specimen was used to prepare seven panel members covering the intermediate - and lower levels of the linear range.

Each panel member was tested in 36 replicates (12 replicates for each of three lots of **cobas**® SARS-CoV-2 Duo reagents), and the results of the study are presented in Figure 3.

**cobas**® SARS-CoV-2 Duo was demonstrated to be linear from 1.0E+02 IU/mL to 1.0E+09 IU/mL and shows a maximum

deviation from linearity of less or equal than ± 0.3 $log_{10}$. Across the linear range, the accuracy of the test was within ± 0.5 $log_{10}$. The lower limit of quantitation (LLoQ) was set and verified at 100 IU/mL.

**Figure 3** Linear range determination




## Lower limit of quantification

The analysis for LLoQ was performed with data obtained from the LoD study at the concentration level of 100 IU/mL. The LLoQ is the lowest titer within the linear range that is not lower than the LoD and meets the acceptance criterion for the Total Analytical Error (|Bias| + 2x SD) (TAE) in alignment with the CLSI EP-17A guideline. The TAE criterion is ≤ 1 $log_{10}$. The results of calculation and claimed LLoQ are shown in Table 13. The LLoQ is 100 IU/mL.

**Table 13** Lower Limit of Quantitation (LLoQ) of **cobas**® SARS-CoV-2 Duo using the WHO International Standard for SARS-CoV-2 Virus (NIBSC code 20/146)

| Lot | Nominal concentration (IU/mL) | $log_{10}$ titer nominal | Mean $log_{10}$ titer observed | SD ($log_{10}$) | Absolute Bias | TAE Absolute bias plus 2 x SD | Difference between measurements SD (=SQRT(2) x 2xSD)* |
|---|---|---|---|---|---|---|---|
| Lot 1 | 100 | 2 | 2.19 | 0.13 | 0.19 | 0.44 | 0.35 |
| Lot 2 | 100 | 2 | 2.11 | 0.12 | 0.11 | 0.36 | 0.35 |
| Lot 3 | 100 | 2 | 2.02 | 0.12 | 0.02 | 0.26 | 0.34 |
| 3 Lots combined | 100 | 2 | 2.11 | 0.14 | 0.11 | 0.39 | 0.4 |

*SD = Standard deviation; sqrt = square root

## SARS-CoV-2 variants verification

The performance of **cobas**® SARS-CoV-2 Duo on SARS-CoV-2 was evaluated by:

- Inclusivity - Verification of the limit of detection
- Verification of the linear range

Table 14 shows the tested SARS-CoV-2 variants.

**Table 14** Overview of tested SARS-CoV-2 variants

| SARS-CoV-2 variants | Lineage number |
|---|---|
| US-WA 1/2020 | USA-WA1/2020 |
| Alpha | Lineage B.1.1.7 |
| Beta | Lineage B.1.351 |
| Gamma | Lineage P.1 |
| Delta | Lineage B.1.617.2 |
| Omicron BA.1 | Lineage B.1.1.529.1 |
| Omicron BA.2 | Lineage B.1.1.529.2 |

### Inclusivity

Cultured isolates of SARS-CoV-2 variants (shown in Table 14) were diluted to two different concentration levels (1 x LoD and 0.5 x LoD). Testing was performed with 63 replicates for each level (21 replicates per each of three lots of **cobas**® SARS-CoV-2 Duo reagents). These results (shown in Table 15) verify that **cobas**® SARS-CoV-2 Duo detects seven different SARS-CoV-2 variants at a concentration of 24.1 IU/mL with a hit rate of ≥ 95%.

**Table 15** Summary of Hit Rates for SARS-CoV-2 Strains (Variants)

| Strain (Variant) | Concentration | Number of Positives/ Number of Valid Replicates | Hit Rate [%] | Mean Target Ct |
|---|---|---|---|---|
| SARS-CoV-2 US-WA1/2020 | ~ 1 x LoD | 63/63 | 100 | 38.2 |
| | ~ 0.5 x LoD | 57/63 | 90.5 | 38.8 |
| SARS-CoV-2 Alpha Variant (Lineage B.1.1.7) | ~ 1 x LoD | 63/63 | 100 | 38.5 |
| | ~ 0.5 x LoD | 53/63 | 84.1 | 39.3 |
| SARS-CoV-2 Beta Variant (Lineage B.1.351) | ~ 1 x LoD | 61/63 | 96.8 | 38.4 |
| | ~ 0.5 x LoD | 44/63 | 69.8 | 39.3 |
| SARS-CoV-2 Gamma Variant (Lineage P.1) | ~ 1 x LoD | 63/63 | 100 | 38.3 |
| | ~ 0.5 x LoD | 55/63 | 87.3 | 39.3 |
| SARS-CoV-2 Delta Variant (Lineage B.1.617.2) | ~ 1 x LoD | 60/63 | 95.2 | 38.5 |
| | ~ 0.5 x LoD | 47/63 | 74.6 | 39.2 |
| SARS-CoV-2 Omicron Variant BA.1 (Lineage B.1.1.529.1) | ~ 1 x LoD | 63/63 | 100 | 37.6 |
| | ~ 0.5 x LoD | 59/63 | 93.7 | 38.5 |
| SARS-CoV-2 Omicron Variant BA.2 (Lineage B.1.1.529.2) | ~ 1 x LoD | 61/63 | 96.8 | 37.8 |
| | ~ 0.5 x LoD | 61/63 | 96.8 | 38.8 |

### Verification of linearity for SARS-CoV-2 variants

For the linearity verification of **cobas**® SARS-CoV-2 Duo, cell-free culture fluid (heat-inactivated) of SARS-CoV-2 USA-WA1/2020 strain, Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2) variants and isolates of Omicron BA.1 (B.1.1.529.1) and Omicron BA.2 (B.1.1.529.2) variant were respectively used in serial dilution spanning the linear range of the assay. Testing was conducted with three lots of **cobas**® SARS-CoV-2 Duo reagent; 12 replicates per level (4 replicates per lot) were tested.

The linear range of **cobas**® SARS-CoV-2 Duo was verified for seven SARS-CoV-2 variants (shown in Table 14). All tested SARS-CoV-2 variants were linear; the maximum mean deviation from linearity was equal to or less than ± 0.3 $\log_{10}$, as shown in Table 16.

**Table 16** Maximum Mean Deviation from Linearity for SARS-CoV-2 Strains (Variants)

| Strain (Variant) | Predicted* value at Maximum Mean Deviation [log10] | Maximum Mean Deviation (observed – predicted*) [log10] | Deviation (Maximum Mean Deviation/predicted*) [%] |
|---|---|---|---|
| SARS-CoV-2 US-WA1/2020 | 2.10 | 0.20 | 9.39 |
| SARS-CoV-2 Alpha Variant (Lineage B.1.1.7) | 2.06 | 0.17 | 8.40 |
| SARS-CoV-2 Beta Variant (Lineage B.1.351) | 2.02 | 0.16 | 7.78 |
| SARS-CoV-2 Gamma Variant (Lineage P.1) | 2.04 | 0.21 | 10.44 |
| SARS-CoV-2 Delta Variant (Lineage B.1.617.2) | 2.02 | 0.26 | 12.75 |
| SARS-CoV-2 Omicron Variant BA.1 (Lineage B.1.1.529.1) | 5.95 | 0.11 | 1.85 |
| SARS-CoV-2 Omicron Variant BA.2 (Lineage B.1.1.529.2) | 3.30 | -0.26 | -7.75 |

*weighted least square regression (1st order)

## Matrix equivalency

Equivalence between nasopharyngeal swabs and nasal swabs was evaluated using the WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146). The WHO International Standard was used to formulate panels to a target concentration of approximately 2 x LoD and 5 x LLoQ into pooled negative clinical samples of each sample type, stabilized in UTM-RT. Twenty-one replicates per concentration were tested for each sample type. All replicates tested with 2 x LoD panel were positive for both matrices with equal or more than 95% hit rate. The difference of the mean log titer for each matrix for 5 x LLoQ panel did not exceed 0.5 log compared to the nominal log titer.

## Analytical specificity (cross-reactivity and microbial interference)

A panel of 43 viruses, bacteria, and fungi (including those commonly found in respiratory tract) were tested with **cobas**® SARS-CoV-2 Duo to assess analytical specificity. The organisms listed in Table 17 were spiked at concentrations of 1 x $10^5$ units/mL for viruses and 1 x $10^6$ units/mL for other organisms, unless otherwise noted. Testing was performed with each potential interfering organism in the absence and presence of SARS-CoV-2 target spiked at ~3 x LoD and 5 x LLoQ. Negative results were obtained with **cobas**® SARS-CoV-2 Duo for all microorganism samples

without SARS-CoV-2 target and positive results were obtained on all of the microorganism samples with SARS-CoV-2 target spiked at ~3 x LoD.

Furthermore, the accuracy of **cobas**® SARS-CoV-2 Duo was not affected when samples spiked with the selected cross reactants were tested at 5 x LLoQ spiked SARS-CoV-2 as the mean $\log_{10}$ titer of each sample was within ± 0.5 $\log_{10}$ of the mean $\log_{10}$ titer of the respective spike control.

**Table 17** Microorganisms tested for analytical specificity/cross reactivity

| **Microorganism** | **Final Test Concentration** |
|---|---|
| Adenovirus (AdV-1) | 1.0E+05 $TCID_{50}$/mL |
| *Bordetella pertussis* | 1.0E+06 CFU/mL |
| *Candida albicans* | 1.0E+06 CFU/mL |
| *Chlamydia pneumoniae* | 7.9E+04 $TCID_{50}$/mL |
| *Corynebacterium diphtheriae* | 1.0E+06 CFU/mL |
| Cytomegalovirus | 1.0E+05 IU/mL |
| Enterovirus (EV68) | 1.0E+05 $TCID_{50}$/mL |
| Epstein Barr Virus | 1.0E+05 cp/mL |
| *Escherichia coli* | 1.0E+06 CFU/mL |
| *Haemophilus influenzae* | 1.0E+06 CFU/mL |
| Human coronavirus 229E | 1.0E+05 $TCID_{50}$/mL |
| Human coronavirus HKU1 | 1.0E+05 genome cp/mL |
| Human coronavirus NL63 | 8.50E+03 $TCID_{50}$/mL |
| Human coronavirus OC43 | 1.0E+05 $TCID_{50}$/mL |
| Human Metapneumovirus | 1.0E+05 $TCID_{50}$/mL |
| Human Rhinovirus | 1.0E+05 PFU/mL |
| Influenza A (H3N2) | 1.0E+05 $TCID_{50}$/mL |
| Influenza B | 1.0E+05 $TCID_{50}$/mL |
| *Lactobacillus acidophilus (for Lactobacillus sp.)* | 1.0E+06 CFU/mL |
| *Legionella longbeachae (for Legionella non-pneumophila)* | 1.0E+06 CFU/mL |
| *Legionella pneumophila* | 1.0E+06 CFU/mL |
| Measles virus | 1.0E+05 $TCID_{50}$/mL |
| MERS-coronavirus | 1.0E+05 cp/mL |
| *Moraxella catarrhalis* | 1.0E+06 CFU/mL |
| Mumps Virus | 1.0E+05 U/mL |
| *Mycobacterium bovis (for Mycobacterium tuberculosis* complex*)* | 1.0E+06 CFU/mL |
| *Mycoplasma pneumoniae* | 1.0E+06 CCU/mL |
| *Neisseria elongata* | 1.0E+06 CFU/mL |
| *Neisseria meningitidis* | 1.0E+06 CFU/mL |
| Parainfluenza virus 1 | 1.0E+05 $TCID_{50}$/mL |
| Parainfluenza virus 2 | 1.0E+05 $TCID_{50}$/mL |
| Parainfluenza virus 3 | 1.0E+05 $TCID_{50}$/mL |

| **Microorganism** | **Final Test Concentration** |
|---|---|
| Parainfluenza virus 4 | 1.0E+05 $TCID_{50}$/mL |
| Parechovirus | 1.0E+05 U/mL |
| *Pneumocystis jirovecii* | 5.0E+03 organisms/mL |
| *Pseudomonas aeruginosa* | 1.0E+06 CFU/mL |
| Respiratory Syncytial Virus | 1.0E+05 PFU/mL |
| SARS-coronavirus (SARS-CoV-1) | 1.0E+05 PFU/mL |
| *Staphylococcus aureus* | 1.0E+06 CFU/mL |
| *Staphylococcus epidermidis* | 1.0E+06 CFU/mL |
| *Streptococcus pneumoniae* | 1.0E+06 CFU/mL |
| *Streptococcus pyogenes* | 1.0E+06 CFU/mL |
| *Streptococcus salivarius* | 1.0E+06 CFU/mL |
| Spike Control | unspiked |

# Clinical performance evaluation

The performance of **cobas**® SARS-CoV-2 Duo was evaluated at one site using archived nasopharyngeal (NPS) and nasal swab (NS) samples from patients with signs and symptoms of a respiratory infection, collected in Copan UTM-RT or BD™ UVT. Clinical samples were collected by qualified personnel according to the package insert of the collection device. Results of **cobas**® SARS-CoV-2 Duo were compared to an EUA authorized highly sensitive SARS-CoV-2 RT-PCR test. The clinical evaluation study included a total of 60 clinical specimens (30 NPS and 30 NS) with 20% low positive samples with comparator Ct values that were within 2-3 Cts of the mean Ct value at the established comparator LoD. For the NPS and NS samples combined the NPA was 100% (95% Score CI: 88.6 - 100%) and the PPA was 100% (95% Score CI: 88.6 - 100%) (Table 18). The NPA and PPA for the NPS samples and NS samples respectively are shown in Table 19.

**Table 18** Performance of the **cobas**® SARS-CoV-2 Duo against an EUA authorized highly sensitive comparator test for NPS and NS combined

| Percent Agreement | Result | LCL 95% Score CI | UCL 95% Score CI |
|---|---|---|---|
| PPA | 100% (30/30) | 88.6% | 100% |
| NPA | 100% (30/30) | 88.6% | 100% |

**Table 19** Performance of **cobas**® SARS-CoV-2 Duo against an EUA authorized highly sensitive comparator test for NPS and NS respectively

| Percent Agreement | Result | LCL 95% Score CI | UCL 95% Score CI |
|---|---|---|---|
| PPA NPS | 100% (15/15) | 79.6% | 100% |
| NPA NPS | 100% (15/15) | 79.6% | 100% |
| PPA NS | 100% (15/15) | 79.6% | 100% |
| NPA NS | 100% (15/15) | 79.6% | 100% |

# Additional information

## Key test features

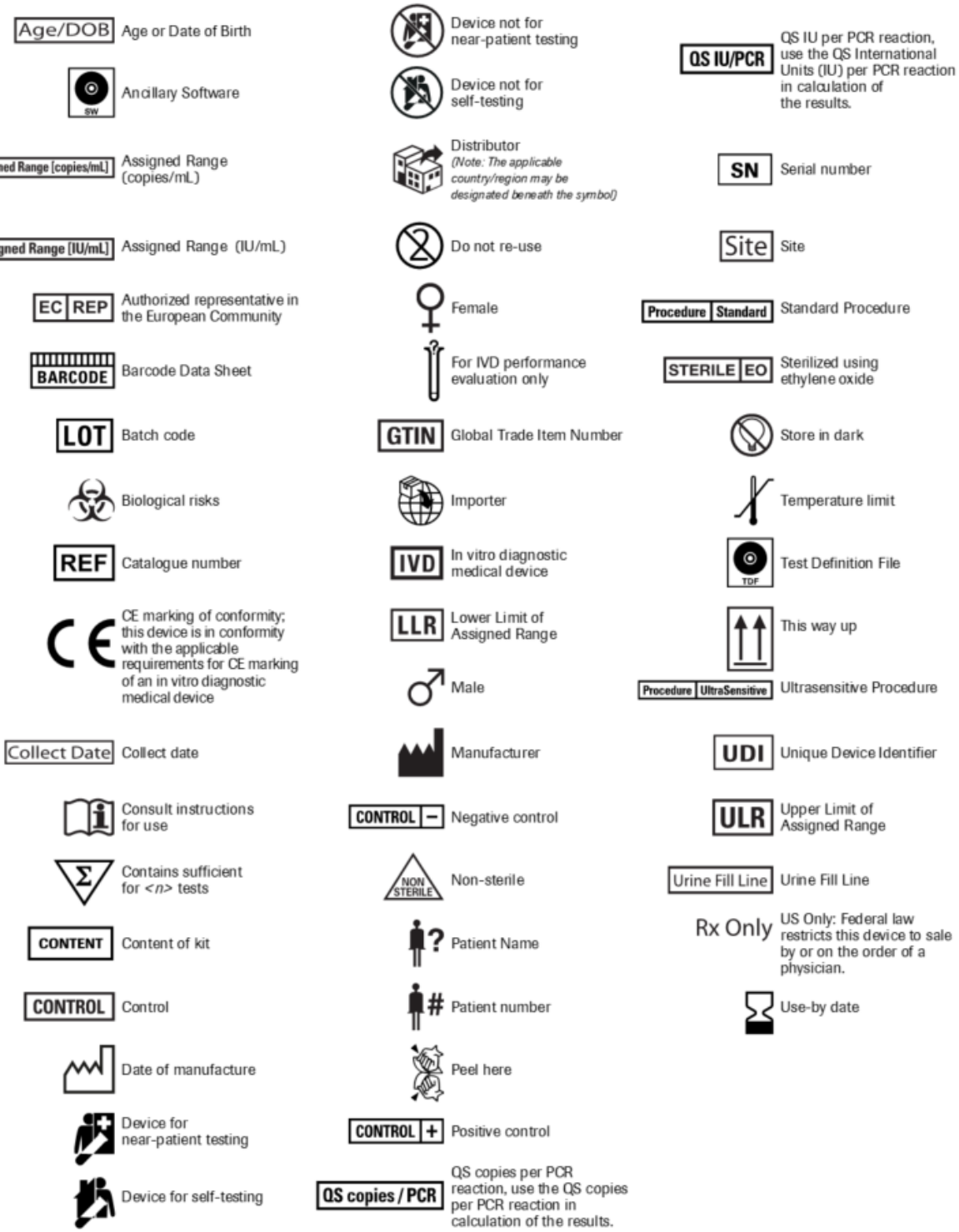
| | |
|---|---|
| **Sample type** | Nasopharyngeal swab samples collected in the Copan UTM-RT System or the BD™ UVT System<br>Nasal swab samples collected in the Copan UTM-RT System or the BD™ UVT System |
| **Minimum amount of sample required** | 0.6 mL* |
| **Sample processing volume** | 0.4 mL |

*Dead volume of 0.2 mL should be considered for the **cobas omni** Secondary tubes. Other tubes compatible with **cobas**® 6800/8800 Systems (consult User Assistance Guide) may have different dead volume and require more or less minimum volume.

# Symbols

**The following symbols are used in labeling for Roche PCR diagnostic products.**

**Table 20** Symbols used in labeling for Roche PCR diagnostics products



## Technical support

For technical support (assistance) please reach out to your local affiliate:
https://www.roche.com/about/business/roche_worldwide.htm

## Manufacturer and distributor

**Table 21** Manufacturer and distributor

Roche Molecular Systems, Inc.
1080 US Highway 202 South
Branchburg, NJ 08876 USA
www.roche.com

Made in USA

Distributed by

Roche Diagnostics
9115 Hague Road
Indianapolis, IN 46250-0457 USA
(For Technical Assistance call the
Roche Response Center
toll-free: 1-800-526-1247)

## Trademarks and patents

See http://www.roche-diagnostics.us/patents

## Copyright

## References

1. Centers for Disease Control and Prevention. Biosafety in Microbiological and Biomedical Laboratories, 6th ed. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institutes of Health HHS Publication No. (CDC) 300859, revised June 2020.

2. Clinical and Laboratory Standards Institute (CLSI). Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline, 4th ed. CLSI Document M29-A4. Wayne, PA: CLSI, 2014.

# Document revision

| Document Revision Information | |
|---|---|
| Doc Rev. 1.0<br>06/2022 | First Publishing. |

# cobas® SARS-CoV-2 Duo

IVD

Rx Only

KIT LOT

## For USA: Emergency Use Authorization only

**cobas® 6800/8800**

SW

**cobas®** SARS-CoV-2 Duo ASAP Version 12.1.1 or higher

**cobas®** 6800/8800 System Software Version 1.4 or higher

This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories. This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

website: http://e-labdoc.roche.com
Product No.: 09500111190
09626867001-01 Doc Rev. 1.0

Please contact your local Roche representative at 1-800-526-1247 if you require a printed copy free of charge or need technical support to access the package insert.

Roche Molecular Systems, Inc.
1080 US Highway 202 South
Branchburg, NJ 08876 USA

09626875001-02